Bloodstream infections in patients with haematological malignancies

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Introduction and Objective:

The risk-assessment for infections in hematological patients with neutropenia, according to IDSA guidelines have been done as high risk (prolonged neutropenia, >7 days; neutrophils count ≤ 100/mm3; substantial concurrent comorbidity; clinically unstable) and low risk (neutropenia expected to resolve within 7 days). Whereas Gram-negative bacteria (*E. coli, Klebsiella spp.* , and *P. aeruginosa*) predominated in neutropenic cancer patients in the 1970s and early 1980s, Gram-positive bacteria (coagulase-negative staphylococci and viridans streptococci) became gradually in the ascendant in the late 1980s and early 1990s. Candidemia is still a serious disease in the hematological patients, although incidence of candidemia has reduced with the introducing of azole drugs in the 1990' s. The empirical antifungal drug is recommended to be taken into consideration in patients with high-risk who have persistent fever over 4–7 days of a broad-spectrum antibacterial therapy and no identified source of fever.

The primary objective of this study was to report the incidence of bloodstream infections (BSIs) and clinically or microbiologically proven bacterial or fungal BSIs during neutropenic episodes in patients with hematological malignancies. BSIs were focused on this study.

Material and method:

In this retrospective observational study**,** all patients older than 14 years who developed febrile neutropenia during chemotherapy for hematological cancers in the hematology department between November 2010 and November 2012 were evaluated. In our hospital, the management of FN was based on the clinical practice guidelines of both the Infectious Diseases Society of America (IDSA) and the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) [1,7,8]. A scoring system for risk of complications among febrile neutropenic patients was based on Multinational Association for Supportive Care in Cancer (MASCC) score.

Table 1. Hematologic malignancies of the patients

Hematologic Malignancies	n (%)
Acute myeloblastic leukemia	73 (58)
Acute lymphocytic leukemia	22 (17)
Non-Hodgkin lymphoma	7 (5)
Chronic lymphocytic leukemia	5 (4)
Multiple myeloma	5 (4)
Hairy cell leukemia	4 (3)
Aplastic anemia	3 (2)
Chronic myeloid leukemia	2 (2)
Plasma cell leukemia	2 (2)
Mantle-cell lymphoma	2 (2)
Chronic lymphocytic leukemia with Burkitt's lymphoma	1 (1)
Total	126 (100)

Table. 2: Isolated bacteria from bloodstream infections of the hematological patients

	(n, %)	Fatal isolate (n)
Extended-spectrum beta-lactamases (-) *E.coli*	14; 21	2
Extended-spectrum beta-lactamases (-) *K.pneumoniae*	8; 12	
Vancomycin-sensitive *Enterococcus faecalis*	6; 9	3
Carbapenem-sensitive *P.aeruginosa*	6; 9	
Extended-spectrum beta-lactamases (+) *K.pneumoniae*	5; 8	
Carbapenem-resistant *Acinetobacter baumannii*	4; 6	2
Methicillin-resistant *S. aureus*	4; 6	2
Extended-spectrum beta-lactamases (+) *E.coli*	3; 5	
Methicillin-sensitive *S. aureus*	2, 3	
Vancomycin-resistant *Enterococcus faecium*	2, 3	1
Vancomycin-sensitive *Enterococcus faecium*	2; 3	1
Ochrobactrum anthropi	1; 1,5	
Methicillin-resistant coagulase-negative staphylococci	1; 1,5	
Extended-spectrum beta-lactamases (-) *K.oxytoca*	1; 1,5	
Stenotrophomonas maltophilia	1; 1,5	
Carbapenem-resistant *P. aeruginosa*	1; 1,5	1
Carbapenem-resistant *S.marcescens*	1; 1,5	
Serratia marcescens	1; 1,5	
Serratia ficaria	1; 1,5	
Citrobacter koseri	1; 1,5	
Enterobacter cloacae	1; 1,5	
Total	**66, 100**	

Results:

During the study period, 15 of 141 patients, who admitted to the hematology ward and were ineligible for study criteria, were excluded. A total of 282 febrile episodes of 126 consecutive patients with neutropenia was retrospectively analyzed during the study period, with 65 cases examined in the first year and 78 in the second year. The mean age was 51.73 ± 14.4 years (range: 17–82 years) and 60 patients were female. The mean MASCC score was 17.18 ± 8.27 (Table 1). The mean duration of FN was 29.38 ± 6.95 days. During 282 febrile episodes in 126 patients, 66 (23%) episodes of bacteremia and 24 (8%) episodes of fungemia were recorded in 48 (38%) and 18 (14%) patients, respectively (Table 1,2, 3).

Table 3. Fungal pathogens and treatment responses of the patients with bloodstream infections: 1-10 cases were in the first year, 11-18 cases were in the second year.

Patient	Age	Gender	Hematologic malignancy	Sample	Fungal pathogen	Antifungal Resistance	History of azole exposure	Empirical antifungal treatment before identification	Treatment modification	Outcome
1	32	Male	AML	Blood	*Candida parapsilosis*	VOR, FLC	+	CAS	-	Survived
				Blood	*Candida parapsilosis*	VOR, FLC	+	CAS	-	Survived
				Blood	*Candida glabrata*	FLC	+	L-AmB	Central line removed	Survived
2	51	Male	AML	Blood	*Candida parapsilosis*	VOR, FLC	+	CAS	Central line removed	Survived
				Blood, Wound	*Candida parapsilosis*	VOR, FLC	+	VOR	From VOR to AM-B	Died
3	32	Male	AML	Blood	*Candida parapsilosis*	VOR, FLC	+	CAS	-	Survived
				Blood	*Candida parapsilosis*	VOR, FLC	+	VOR	From VOR to L-AmB	Survived
4	52	Female	ALL	Blood	*Geotrichum capitatum*	FLC, ITR	-	CAS	Central line removed	Survived
				Blood	*Geotrichum capitatum*	FLC, ITR	+	VOR	-	Died
5	60	Female	ALL	Blood	*Candida albicans*	VOR, ITR, FLC	-	CAS	-	Survived
6	21	Female	Aplastic Anemia	Blood	*Candida albicans*		-	CAS	-	Survived
7	33	Male	AML	Blood	*Geotrichum capitatum*	FLC	-	VOR	Central line removed	Survived
8	55	Female	AML	Blood	*Trichosporon asahii*	AmB	+	CAS	Central line removed	Died
9	63	Female	AML	Blood	*Trichosporon asahii*	AmB	+	L-AmB	From AM-B to VOR, central line removed	Died
10	45	Female	AML	Blood	*Trichosporon asahii*	AmB, ITR	-	CAS	Empirically switched to VOR	Died
11	50	Male	AML+Lung Cancer	Blood	*Candida parapsilosis*		+	VOR	From VOR to AM-B, central line removed	Survived
				Blood	*Candida albicans*	-	+	VOR	-	Survived
12	62	Female	AML	Blood, Sputum	*Candida parapsilosis*		+	VOR	From VOR to CAS, central line removed	Died
13	61	Male	AML	Blood, Urine	*Candida albicans*		+	CAS		Died
14	73	Female	NHL	Blood, Central Line	*Candida albicans*		+	L-AmB	Central line removed	Survived
15	35	Male	AML	Blood	*Candida albicans*		+	CAS		Survived
16	44	Female	ALL	Blood	*Candida albicans*		+	L-AmB		Survived
17	63	Female	AML	Blood	*Candida krusei*		+	VOR	-	Survived
18	51	Female	AML	Blood	*Candida albicans*	-	+	VOR	-	Survived

Abbreviations: AML; Acute myeloblastic leukemia, ALL; Acute lymphocytic leukemia, CLL; Chronic lymphocytic leukemia, NHL; Non-Hodgkin lymphoma, BAL; Bronchoalveolar lavage, VOR; Voriconazole, L-AmB; Liposomal amphotericin B, CAS; Caspofungin, FLC; Fluconazole, ITR; Itraconazole, AmB: Amphotericin B.

Conclusion:

BSIs, which occur during febrile neutropenic episodes in hematological patients due to GNB should be treated initially with non-carbapenem based anti-pseudomonal therapy taking into antimicrobial stewardship. Non-azole antifungal drugs, including caspofungin, liposomal Amphotericin B, etc. should be preferred as empirical antifungal therapy in case of possible or probable invasive fungal infection with absence of pulmonary findings due to increase azole resistance.